GBA gene

glucosylceramidase beta

Normal Function

The *GBA* gene provides instructions for making an enzyme called beta-glucocerebrosidase. This enzyme is active in lysosomes, which are structures inside cells that act as recycling centers. Lysosomes use digestive enzymes to break down toxic substances, digest bacteria that invade the cell, and recycle worn-out cell components. Based on these functions, enzymes in the lysosome are sometimes called housekeeping enzymes. Beta-glucocerebrosidase is a housekeeping enzyme that helps break down a large molecule called glucocerebroside into a sugar (glucose) and a simpler fat molecule (ceramide).

Health Conditions Related to Genetic Changes

Gaucher disease

More than 200 mutations in the *GBA* gene have been identified in people with Gaucher disease, a disorder with varied features that affect many parts of the body. These mutations occur in both copies of the gene in each cell. Most of the *GBA* mutations responsible for Gaucher disease change a single protein building block (amino acid) in beta-glucocerebrosidase, altering the structure of the enzyme and preventing it from working normally. Other mutations delete or insert genetic material in the *GBA* gene or lead to the production of an abnormally short, nonfunctional version of the enzyme.

Mutations in the *GBA* gene greatly reduce or eliminate the activity of beta-glucocerebrosidase in cells. As a result, glucocerebroside is not broken down properly. This molecule and related substances can build up in white blood cells called macrophages in the spleen, liver, bone marrow, and other organs. The abnormal accumulation and storage of these substances damages tissues and organs, causing the characteristic features of Gaucher disease.

Parkinson disease

Changes in the *GBA* gene are also associated with Parkinson disease and parkinsonism, which are similar disorders that affect movement and balance. People with Gaucher disease have mutations in both copies of the *GBA* gene in each cell, while those with a mutation in just one copy of the gene are called carriers. People with Gaucher disease and people who are carriers of a *GBA* gene mutation have an increased risk of developing Parkinson disease or parkinsonism.

Symptoms of Parkinson disease and parkinsonism result from the loss of nerve cells that produce dopamine. Dopamine is a chemical messenger that transmits signals within the brain to produce smooth physical movements. It remains unclear how *GBA* gene mutations are related to these disorders. Studies suggest that changes in this gene may contribute to the faulty breakdown of toxic substances in nerve cells by impairing the function of lysosomes. Alternatively, the changes may increase the formation of abnormal protein deposits. As a result, toxic substances or protein deposits could accumulate and kill dopamine-producing nerve cells, leading to abnormal movements and balance problems.

other disorders

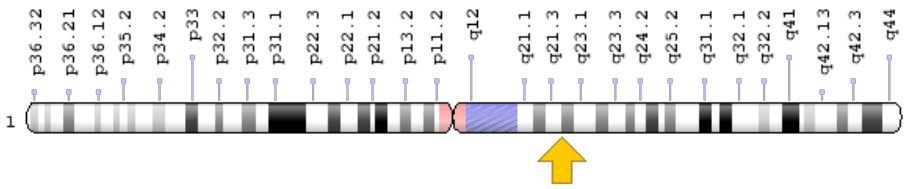
Research suggests an association between *GBA* gene mutations and a disorder called dementia with Lewy bodies. Lewy bodies are abnormal deposits of the protein alpha-synuclein that form in some dead or dying nerve cells. Specifically, they occur in nerve cells that produce the chemical messenger dopamine. The features of this disorder are variable, but symptoms typically include a loss of intellectual functions (dementia), visual hallucinations, and changes in alertness and attention. Affected individuals may have features characteristic of Parkinson disease such as trembling or rigidity of limbs, slow movement, and impaired balance and coordination. Lewy bodies are also a feature of Parkinson disease, but these abnormal deposits tend to be more widespread in the brain in dementia with Lewy bodies.

Carriers of *GBA* gene mutations appear to have an increased risk of developing dementia with Lewy bodies, although it remains unclear how changes in this gene increase the risk. Researchers speculate that mutations in the *GBA* gene alter the structure of beta-glucocerebrosidase and impair the function of lysosomes. As a result, alpha-synuclein may not be processed properly, allowing the formation of Lewy bodies.

Chromosomal Location

Cytogenetic Location: 1q22, which is the long (q) arm of chromosome 1 at position 22

Molecular Location: base pairs 155,234,448 to 155,244,862 on chromosome 1 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- Acid beta-glucosidase
- Alglucerase
- beta-D-glucosyl-N-acylsphingosine glucohydrolase
- Beta-glucocerebrosidase
- D-Glucosyl-N-acylsphingosine glucosylhydrolase
- GBA1
- GLCM_HUMAN
- GLUC
- Glucocerebrosidase
- Glucocerebroside beta-Glucosidase
- glucosidase, beta, acid
- glucosidase, beta; acid (includes glucosylceramidase)
- glucosphingosine glucosylhydrolase
- Glucosylceramidase
- Glucosylceramide beta-Glucosidase
- Imiglucerase

Additional Information & Resources

Educational Resources

- HuGENet Case Study: Glucocerebrosidase Gene Mutations and Parkinson's Disease
  https://www.cdc.gov/genomics/hugenet/CaseStudy/PARKINSON/PARKview.htm
- National Institute of Neurological Disorders and Stroke: Dementia with Lewy Bodies
  https://www.ninds.nih.gov/Disorders/All-Disorders/Dementia-Lewy-Bodies-Information-Page
- NIH News Release: Researchers Uncover Genetic Clues to a Common Form of Age-Related Dementia (July 17, 2006)
  https://www.genome.gov/19517231/

GeneReviews

- Gaucher Disease
  https://www.ncbi.nlm.nih.gov/books/NBK1269

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28GBA%5BTI%5D%29+OR+%28beta+glucosidase%5BTIAB%5D%29+OR+%28glucosylceramidase%5BTIAB%5D%29+OR+%28Glucocerebrosidase%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D

OMIM

- DEMENTIA, LEWY BODY
  http://omim.org/entry/127750
- GLUCOSIDASE, BETA, ACID
  http://omim.org/entry/606463

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_GBA.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=GBA%5Bgene%5D
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=4177
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/2629
- PDGene
  http://www.pdgene.org/view?gene=GBA
- UniProt
  http://www.uniprot.org/uniprot/P04062

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